WEST Search History

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Hide?	Set Name	Query	Hit Count
		DB=USPT; PLUR=YES; OP=OR	
☐	L49	5798225.pn.	1
☐	L48	5695955.pn.	1
☐	L47	5693616.pn.	1
☐	L46	5584592.pn.	1
☐	L45	5395824.pn.	1
☐	L44	5149779.pn.	1
		DB=DWPI; PLUR=YES; OP=OR	
☐	L43	9918945	2
		DB=EPAB; PLUR=YES; OP=OR	
☐	L42	WO-9851329-A1.did.	1
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☐	L41	9851329	2
		DB=USPT; PLUR=YES; OP=OR	
☐	L40	L37 and (PTHrP)adj(antibod?)	2
☐	L39	L37 and PTHrP	17
☐	L38	L37 and anti-PTHrP	2
☐	L37	424/130.1, 133.1, 134.1, 145.1, 178.1.ccls.	9230
		DB=EPAB; PLUR=YES; OP=OR	
☐	L36	WO-9633735-A1.did.	1
		DB=DWPI; PLUR=YES; OP=OR	
☐	L35	9633735	1
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR	
☐	L34	(arginine)adj(vasopressin)adj(levels)	3
☐	L33	L32 and antibod?	7
☐	L32	L31 and treatment	84
☐	L31	(vasopressin)adj(level)	92
☐	L30	L29 and diabetes	41
☐	L29	L20 and hypercalcemia	42
☐	L28	(FERM)adj(BP-5631)	10
☐	L27	L24 and treatment	40
☐	L26	L25 and vasopressin	3

☐	L25	L24 and cancer	36
☐	L24	anti-PTHrP	47
☐	L23	L20 and (parathyroid)adj(hormone)adj(related)adj(protein)	2
☐	L22	L20 and anti-PTHrP	0
☐	L21	L20 and PTHrP	3
☐	L20	(vasopressin)same(cancer)	541
☐	L19	L18 and vasopressin	28
☐	L18	(azuma)adjadj(yumiko)	35021
☐	L17	(tsunenari)adj(toshiaki)	23
☐	L16	(onuma)adj(etsuro)	6
☐	L15	L14 and vassopressin	0
☐	L14	(ogata)adj(etsuro)	17
☐	L13	(vassopressin)same(PTHrP)same(antibod?)	0
☐	L12	(vassopressin)same(anti-PTHrP)	0
☐	L11	L10 and anti-PTHrP	2
☐	L10	(vasopressin)same(parathyroid)adj(hormone)adj(related)adj(peptide)	31
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☐	L9	4-228089	0
☐	L8	jp 4228089	7843469
	DB=JPAB,DWPI; PLUR=YES; OP=OR		
☐	L7	jp 4228089	15699870
	DB=JPAB; PLUR=YES; OP=OR		
☐	L6	4228089	0
	DB=EPAB; PLUR=YES; OP=OR		
☐	L5	WO-9217602-A1.did.	1
	DB=DWPI; PLUR=YES; OP=OR		
☐	L4	9217602	2
	DB=EPAB; PLUR=YES; OP=OR		
☐	L3	EP-962467-A1.did.	1
	DB=DWPI; PLUR=YES; OP=OR		
☐	L2	9813388	2
	DB=USPT; PLUR=YES; OP=OR		
☐	L1	5001223.pn.	1

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NEWS 7	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 8	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 9	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
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NEWS 20	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 21	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 22	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 23	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 24	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 25	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 26	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 27	DEC 18	CA/CAplus patent kind codes updated
NEWS 28	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 29	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 30	DEC 27	CA/CAplus enhanced with more pre-1907 records

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE 'HOME' ENTERED AT 10:06:38 ON 27 DEC 2006

=> file medline embase biosis scisearch caplus
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FILE 'EMBASE' ENTERED AT 10:06:55 ON 27 DEC 2006

FILE 'BIOSIS' ENTERED AT 10:06:55 ON 27 DEC 2006

FILE 'SCISEARCH' ENTERED AT 10:06:55 ON 27 DEC 2006

FILE 'CAPLUS' ENTERED AT 10:06:55 ON 27 DEC 2006

=> s low vasopressin
L1 53 LOW VASOPRESSIN

=> s l1 and parathyroid hormone
L2 1 L1 AND PARATHYROID HORMONE

=> d l2 cbib abs

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
2001:31353 Document No. 134:114837 Agents for ameliorating low vasopressin level. Ogata, Etsuro; Onuma, Etsuro; Tsunenari, Toshiaki; Saito, Hidemi; Azuma, Yumiko (Chugai Seiyaku Kabushiki Kaisha, Japan). PCT Int. Appl. WO 2001002010 A1 20010111, 114 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP4413 20000703. PRIORITY: JP 1999-189322 19990702.

AB Agents for ameliorating low vasopressin level which contain as the active ingredient a substance capable of inhibiting the binding of a parathyroid hormone-associated peptide to its receptor; and agents for ameliorating symptoms caused by a decrease in vasopressin level which contain as the active ingredient a substance capable of inhibiting the binding of a parathyroid hormone-associated peptide to its receptor.

=> s l1 and treatment
L3 12 L1 AND TREATMENT

=> dup remove l3
PROCESSING COMPLETED FOR L3
L4 4 DUP REMOVE L3 (8 DUPLICATES REMOVED)

=> d l4 1-4 cbib abs

L4 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1
2004255503. PubMed ID: 15118420. Sodium fraction excretion rate in nocturnal enuresis correlates with nocturnal polyuria and osmolality. Aceto Gabriella; Penza Rosa; Delvecchio Maurizio; Chiozza Maria Laura; Cimador Marcello; Caione Paolo. (Department Biomedicina Eta Evolutiva, University, Bari, Italy.) The Journal of urology, (2004 Jun) Vol. 171, No. 6 Pt 2, pp. 2567-70. Journal code: 0376374. ISSN: 0022-5347. Pub. country: United States. Language: English.

AB PURPOSE: We verify the sodium fraction excretion rate (FE Na) and potassium fraction excretion (FE K) rates in monosymptomatic nocturnal enuresis. We also correlate FE Na and FE K to urinary osmolality, nocturnal polyuria and vasopressin in the same population. MATERIALS AND METHODS: A total of 438 children 6 to 15 years old (mean age 9.7) presenting with monosymptomatic nocturnal enuresis were recruited from different centers. Inclusion criteria were 3 or greater wet nights a week, no daytime incontinence and no treatment in the previous 2 months. Exclusion criteria were cardiopathy, endocrinopathy, psychiatric problems and urinary tract abnormalities. Micturition chart, diurnal (8 am to 8 pm) and nocturnal (8 pm to 8 am) urine collection, including separate diuresis volumes, (Na, K and Ca) electrolytes and osmolality were evaluated, as well as serum electrolytes, creatinine and nocturnal (4 am) vasopressin. Diurnal and nocturnal FE K and FE Na were calculated. ANOVA test, chi-square test, Student's t test and Pearson correlation test were used for statistical analysis. RESULTS:: Nocturnal polyuria (diurnal to nocturnal diuresis ratio less than 1) was found in 273 children (62.3%, group 1 and nocturnal urine volumes were normal in 165 with enuresis (37.7%, group 2). Nocturnal FE Na was abnormal in 179 children (40.8%), including 118 in group 1 (43.2%) and 61 in group 2 (36.9%) (chi-square not significant). FE Na was also increased in nocturnal versus daytime diuresis (Student's t test p <0.001). In group 1 nocturnal FE Na correlated with nocturnal diuresis (Pearson correlation p = 0.003, r = +0.175), while daytime FE Na and nocturnal FE Na correlated with diurnal diuresis (Pearson correlation p = 0.001, r = +0.225 and Pearson correlation p = 0.001, r = +0.209, respectively). In group 2 nocturnal FE Na did not correlate with diuresis (Pearson correlation p = 0.103, r = +0.128) but correlated with vasopressin values (Pearson correlation p = 0.042, r = -0.205). Urine osmolality was reduced in 140 children (31.9%) and correlated with nocturnal diuresis (Pearson correlation p = 0.003, r = -0.321). Vasopressin was decreased in 332 children (75.8%, 62.6% in group 1 and 13.2% in group 2). No significant difference was found between sexes and age of enuretic subgroups. CONCLUSIONS: Nocturnal FE Na correlates with nocturnal diuresis, whereas daytime FE Na does not. FE K in daytime and nighttime diuresis does not statistically differ in nocturnal polyuric and nonpolyuric enuretic groups. Osmolality correlates with nocturnal diuresis, and vasopressin at 4 am was lower in the nocturnal polyuric group. The hypothesis of a subset of enuretic patients presenting with nocturnal polyuria associated with high nocturnal natriuria and low vasopressin values has been confirmed.

L4 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 2
1998:2331 Document No.: PREV199800002331. A prospective randomized trial of arginine vasopressin in the treatment of vasodilatory shock after left ventricular assist device placement. Argenziano, Michael;

Choudhri, Asim F.; Oz, Mehmet C. [Reprint author]; Rose, Eric A.; Smith, Craig R.; Landry, Donald W. [Reprint author]. Milstein Hosp. Room 7-435, 177 Fort Washington Ave., New York, NY 10032, USA. Circulation, (Nov. 4, 1997) Vol. 96, No. 9 SUPPL., pp. II286-II290. print.
CODEN: CIRCAZ. ISSN: 0009-7322. Language: English.

AB Background: Vasodilatory shock requiring catecholamine pressors occurs in some patients following cardiopulmonary bypass. Prompted by a clinical observation, we investigated the use of vasopressin as a treatment for this syndrome in a randomized, controlled trial. Methods and Results: Patients undergoing placement of a left ventricular assist device (n=23) were evaluated for postbypass vasodilatory shock requiring catecholamine pressors, and consecutive eligible subjects (n = 10) were evenly randomized to blinded intravenous vasopressin or saline placebo. Vasopressin (0.1 U/min) increased mean arterial pressure (57+-4 to 84+-2 mm Hg, P<.001) and systemic vascular resistance (813+-113 to 1188+-87 dyne-s/cm,5 P<.001), with decreased norepinephrine administration. There was no significant response to saline, but in three subjects who crossed over, blinded vasopressin increased mean arterial pressure (69 +- 8 to 93+-4 mm Hg) and systemic vascular resistance (898+-88 to 1443+-72 dyne-s/cm5) with decreased norepinephrine administration. Plasma vasopressin concentrations prior to randomization clustered in two groups: one (n=5) with concentrations inappropriately low for the degree of hypotension (8.4+-2.1 pg/mL) and a second (n=3) with moderately elevated levels (33.7+-1.6 pg/mL); vasopressin increased mean arterial pressure in the low vasopressin group from 57 +- 4 to 85 + 2 mm Hg (P<.01) and in the high vasopressin group from 68+-8 to 86+-4 mm Hg. Conclusions: Vasopressin is an effective pressor in vasodilatory shock after cardiopulmonary bypass. An absolute vasopressin deficiency was observed in the majority of patients, but all subjects responded to vasopressin administration.

L4 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 3

1998045879. PubMed ID: 9386112. A prospective randomized trial of arginine vasopressin in the treatment of vasodilatory shock after left ventricular assist device placement. Argenziano M; Choudhri A F; Oz M C; Rose E A; Smith C R; Landry D W. (Department of Surgery, Columbia University College of Physicians and Surgeons, New York, NY, USA.) Circulation, (1997 Nov 4) Vol. 96, No. 9 Suppl, pp. II-286-90. Journal code: 0147763. ISSN: 0009-7322. Pub. country: United States. Language: English.

AB BACKGROUND: Vasodilatory shock requiring catecholamine pressors occurs in some patients following cardiopulmonary bypass. Prompted by a clinical observation, we investigated the use of vasopressin as a treatment for this syndrome in a randomized, controlled trial. METHODS AND RESULTS: Patients undergoing placement of a left ventricular assist device (n=23) were evaluated for post-bypass vasodilatory shock requiring catecholamine pressors, and consecutive eligible subjects (n=10) were evenly randomized to blinded intravenous vasopressin or saline placebo. Vasopressin (0.1 U/min) increased mean arterial pressure (57+/-4 to 84+/-2 mm Hg, P<.001) and systemic vascular resistance (813+/-113 to 1188+/-87 dyne-s/cm5, P<.001), with decreased norepinephrine administration. There was no significant response to saline, but in three subjects who crossed over, blinded vasopressin increased mean arterial pressure (69+/-8 to 93+/-4 mm Hg) and systemic vascular resistance (898+/-88 to 1443+/-72 dyne-s/cm5) with decreased norepinephrine administration. Plasma vasopressin concentrations prior to randomization clustered in two groups: one (n=5) with concentrations inappropriately low for the degree of hypotension (8.4+/-2.1 pg/mL) and a second (n=3) with moderately elevated levels (33.7+/-1.6 pg/mL); vasopressin increased mean arterial pressure in the low vasopressin group from 57+/-4 to 85+/-2 mm Hg (P<.01) and in the high vasopressin group from 68+/-8 to 86+/-4 mm Hg. CONCLUSIONS: Vasopressin is an effective pressor in vasodilatory shock after cardiopulmonary bypass. An absolute vasopressin deficiency was observed in the majority of patients, but all subjects responded to vasopressin administration.

L4 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 4
81105539. PubMed ID: 7006294. Hypernatraemia, diabetes mellitus, hyperprolactinaemia, retarded growth and delayed puberty in a 14 year old girl. Effect of bromocriptine treatment. Christensen N C; Hagen C; Nielsen M D; Petersen S. Acta endocrinologica, (1981 Jan) Vol. 96, No. 1, pp. 30-5. Journal code: 0370312. ISSN: 0001-5598. Pub. country: Denmark. Language: English.
AB Investigations in a 14 year old girl with arrested growth for 2 years, delayed pubertal development, hypernatraemia without thirst, diabetes mellitus and hyperlipaemia are reported. The hypernatraemia was accompanied by a low vasopressin concentration with an abnormal response to thirst, high plasma renin but normal plasma aldosterone concentrations. Treatment with vasopressin and increased fluid intake decreased serum sodium levels. Serum gonadotrophins were low; GH response during an insulin tolerance test was subnormal and basal serum Prl concentration was elevated. Bone age, thyroid function and adrenal function were normal. After initiation of bromocriptine treatment her growth accelerated and regular menstruations commenced. The serum gonadotrophin levels increased and showed pulsatile release. A hypothalamic disorder is suggested, but no cerebral lesion could be demonstrated.

=> s vasopressin deficiency
L5 567 VASOPRESSIN DEFICIENCY

=> s l5 and parathyroid hormone
L6 1 L5 AND PARATHYROID HORMONE

=> d l6 cbib abs

L6 ANSWER 1 OF 1 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
79259348 EMBASE Document No.: 1979259348. Dissociation between plasma, urine, and renal papillary cyclic AMP content following vasopressin and DDAVP. Bia M.J.; Dewitt S.; Forrest Jr. J.N.. Renal Sect., Dept. Int. Med., Yale Univ. Sch. Med., New Haven, Conn. 06510, United States. American Journal of Physiology - Renal Fluid and Electrolyte Physiology Vol. 6, No. 3, pp. F218-F225 1979.
CODEN: AJPFDM
Pub. Country: United States. Language: English.
AB The effects of in vivo physiologic doses of vasopressin and 1-deamino-8-D-arginine vasopressin (DDAVP) on the cyclic AMP content of plasma, urine, and renal papillary tissue were determined in the ADH-deficient Brattleboro rat. During clearance studies, plasma cyclic AMP concentrations and both total and nephrogenous urinary cyclic AMP excretion in vasopressin- and DDAVP-treated rats were similar to the values in time-matched controls. In contrast, in situ renal papillary cyclic AMP content was higher ($P<0.001$) in both vasopressin- (35.7 ± 3.6 pmol/mg protein) and DDAVP- (29.7 ± 2.2 pmol/mg protein) treated rats compared to controls (15.1 ± 1.3 pmol/mg protein). Endogenous stimulation of vasopressin by dehydration in normal rats increased both papillary cyclic AMP content (27.1 ± 2.7 pmol/mg protein) and urine osmolality, whereas no change in papillary cyclic AMP was observed following dehydration in Brattleboro rats (13.6 ± 0.8 pmol/mg protein) despite an increase in urine osmolality. The results demonstrate that changes in cyclic AMP following in vivo vasopressin are best demonstrated by measurement of in situ cyclic AMP content of the renal papilla, whereas total urinary cyclic AMP and nephrogenous cyclic AMP are not useful indices of tubular sensitivity to this hormone.

=> s l5 and hypercalcemia
L7 0 L5 AND HYPERCALCEMIA

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=> s l5 and treatment
L8          117 L5 AND TREATMENT

=> s l8 and antibod?
L9            0 L8 AND ANTIBOD?

=> s parathyroid hormone related protein
L10        9998 PARATHYROID HORMONE RELATED PROTEIN

=> s l10 and PTHrP
L11        6896 L10 AND PTHRP

=> s l11 and antibod?
L12         857 L11 AND ANTIBOD?

=> s l12 and vasopressin
L13           3 L12 AND VASOPRESSIN

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14           3 DUP REMOVE L13 (0 DUPLICATES REMOVED)

=> d l14 1-3 cbib abs

L14  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2006 ACS on STN
2001:31353  Document No. 134:114837  Agents for ameliorating low
     vasopressin level.  Ogata, Etsuro; Onuma, Etsuro; Tsunenari,
     Toshiaki; Saito, Hidemi; Azuma, Yumiko (Chugai Seiyaku Kabushiki Kaisha,
     Japan).  PCT Int. Appl. WO 2001002010 A1 20010111, 114 pp.  DESIGNATED
     STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
     CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
     ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
     MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
     SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
     KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK,
     ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD,
     TG.  (Japanese).  CODEN: PIXXD2.  APPLICATION: WO 2000-JP4413 20000703.
     PRIORITY: JP 1999-189322 19990702.
AB   Agents for ameliorating low vasopressin level which contain as
     the active ingredient a substance capable of inhibiting the binding of a
     parathyroid hormone-associated peptide to its receptor; and agents for
     ameliorating symptoms caused by a decrease in vasopressin level
     which contain as the active ingredient a substance capable of inhibiting
     the binding of a parathyroid hormone-associated peptide to its receptor.

L14  ANSWER 2 OF 3  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
2000222942  EMBASE  Parathyroid hormone-related
     protein as a potential target of therapy for cancer-associated
     morbidity. Ogata E.. Dr. E. Ogata, Cancer Institute Hospital, Japanese
     Found. for Cancer Research, 1-37 Kami-Ikebukuro, Toshima-ku, Tokyo 170,
     Japan. Cancer  Vol. 88, No. 12 SUPPL., pp. 2909-2911  15 Jun 2000.
     Refs: 4.
     ISSN: 0008-543X. CODEN: CANCAR
     Pub. Country: United States. Language: English. Summary Language: English.
     Entered STN: 20000713. Last Updated on STN: 20000713
AB   BACKGROUND.  Proinflammatory cytokines are involved in the genesis of
     cancer-associated cachexia.  Parathyroid hormone-
     related protein (PTHrP) is the causative agent
     in humoral hypercalcemia of malignancy (HHM) and is frequently secreted
     from various kinds of solid tumors as well as from adult T-cell
     leukemia/lymphoma.  PTHrP, like PTH, acts on PTH receptor type 1
     (PTH1R).  Activation of PTH1R may lead to stimulation of secretion of
     proinflammatory cytokines.  It is expected, therefore, that PTHrP
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constitutes a key factor in the activation of the proinflammatory and cachectogenic cytokine network and consequently in the development of cachexia in patients with cancer. METHODS. Two groups of cancer-bearing patients of similar clinical backgrounds were enrolled. Plasma concentrations of PTHrP and cytokines were measured with immunoradiometric assay and radioimmunoassay, respectively. Cancer tissues from patients with HHM were transplanted into nude mice or nude rats. The effects of humanized antihuman PTHrP antibody were examined RESULTS. In clinical studies, Group B patients (with elevated plasma PTHrP), compared with Group A patients (with normal plasma PTHrP), tended to exhibit higher plasma levels of tumor necrosis factor (TNF)-α (P = 0.13), interleukin(IL)-5 (P = 0.08), and IL-8 (P = 0.08), and had significantly higher levels of IL-6 (P = ≤0.01). The levels of TNF-α and IL-6 correlated with those of PTHrP. In animal studies, the antibody caused a prompt and sustained decline in serum calcium. This response was accompanied by improvements in food intake, drinking, body weight gain, and general behavior. It also ameliorated the suppression of serum ADH. When those effects were compared with those induced either by bisphosphonate or calcitonin, it turned out that not all of the beneficial effects of the antibody were directly correlated with the depression of blood calcium. CONCLUSIONS. PTHrP is a promising molecular target for the development of a novel mode of treatment for patients with cancer-associated morbidity. (C) 2000 American Cancer Society.

L14 ANSWER 3 OF 3 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

1995:837036 The Genuine Article (R) Number: TJ130. PARATHYROID HORMONE-RELATED PROTEIN IS AN AUTOCRINE MODULATOR OF RABBIT PROXIMAL TUBULE CELL-GROWTH. GARCIAOCANA A (Reprint); DEMIGUEL F; PENARANDA C; ALBAR J P; SARASA J L; ESBRIT P. FDN JIMENEZ DIAZ, UNIDAD METAB LAB, E-28040 MADRID, SPAIN; FDN JIMENEZ DIAZ, DEPT PATHOL, E-28040 MADRID, SPAIN; CSIC, CTR NACL BIOTECNOL, IMMUNOL UNIT, MADRID, SPAIN. JOURNAL OF BONE AND MINERAL RESEARCH (DEC 1995) Vol. 10, No. 12, pp. 1875-1884. ISSN: 0884-0431. Publisher: BLACKWELL SCIENCE PUBL INC CAMBRIDGE, 238 MAIN ST, CAMBRIDGE, MA 02142. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Parathyroid hormone-related protein (PTHrP), a likely mediator for humoral hypercalcemia of malignancy, is also synthesized in various normal tissues. In the kidney, PTHrP, mainly detected in proximal and distal tubules, has been shown to stimulate proliferation of rat mesangial cells in culture. Experiments were carried out to investigate the possible mitogenic effect of PTHrP in cultures of rabbit proximal tubule cells (PTC). Immunocytochemical analysis, using antihuman (h)PTHrP antibodies to (38-64) and (107-111) epitopes in the PTHrP molecule, showed strong cytoplasmic staining in PTC and in proximal tubule-like LLC-PK1 cells. PTC secreted immunereactive PTHrP (54.8 +/- 7.0 fmol/10(6) cells) into the culture medium. Human PTHrP(1-141) stimulated proliferation in subconfluent cultures of these cells dose-dependently. This effect was similar to that induced by [Tyr(34)] hPTHrP(1-34) amide (hPTHrP[1-34]), hPTHrP(1-86), and bovine (b)PTH(1-34), while hPTHrP(38-64) amide, hPTHrP(107-111) amide, and hPTHrP(107-139) amide were ineffective. Addition of anti-hPTHrP neutralizing antibodies to (1-34), (38-64), and (107-111) epitopes of PTHrP decreased PTC growth. The mitogenic effect of these agonists was abolished in confluent PTC. In contrast, [Nle(8,18) Tyr(34)]bPTH(3-34) amide (PTH[3-34]) increased DNA synthesis in either subconfluent or confluent PTC. In LLC-PK1 cells, which also secreted PTHrP and are devoid of PTH receptors, none of these peptides affected proliferation. Forskolin (10 mu M) or H-8 (2 mu M), a protein kinase A inhibitor, did not affect basal or hPTHrP(1-34)-stimulated DNA synthesis, respectively, in subconfluent PTC. On the other hand, 10 nM staurosporine and 100 nM calphostin C, protein kinase C (PKC) inhibitors,

blunted the effects of hPTHrP(1-34) or bPTH(3-34) on DNA synthesis in these cells. These studies suggest that PTHrP may function as an autocrine factor in the regulation of proximal tubule cell growth by a PKC-mediated mechanism.

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L15           0 L12 AND FERM BP-5631

=> s FERM BP-5631
L16           0 FERM BP-5631

=> s hybridoma
L17       73304 HYBRIDOMA

=> s l17 and "FERM BP-5631"
L18           0 L17 AND "FERM BP-5631"

=> s hyperosmolarity
L19        4749 HYPEROSMOLARITY

=> s l19 and vasopressin
L20         186 L19 AND VASOPRESSIN

=> s l20 and treatment
L21          35 L20 AND TREATMENT

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L22  ANSWER 1 OF 21  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
2006217915  EMBASE  Plasma arginine-vasopressin following
     experimental stroke: Effect of osmotherapy. Chang Y.; Chen T.-Y.; Chen
     C.-H.; Crain B.J.; Toung T.J.K.; Bhardwaj A.. A. Bhardwaj, Department of
     Neurology, L-226, Oregon Health and Science University, 3185 SW Sam
     Jackson Park Rd., Portland, OR 97239-3098, United States.
     bhardwaj@ohsu.edu. Journal of Applied Physiology  Vol. 100, No. 5, pp.
     1445-1451  2006.
     Refs: 49.
     ISSN: 8750-7587. E-ISSN: 1522-1601. CODEN: JAPHEV
     Pub. Country: United States. Language: English. Summary Language: English.
     Entered STN: 20060602. Last Updated on STN: 20060602
AB   Neurohumoral responses have been implicated in the pathogenesis of
     ischemia-evoked cerebral edema. In a well-characterized animal model of
     ischemic stroke, the present study was undertaken to 1) study the profile
     of plasma arginine-vasopressin (AVP), and 2) determine whether
     osmotherapy with mannitol and various concentrations of hypertonic saline
     (HS) solutions influence plasma AVP levels. Halothane-anesthetized adult
     male Wistar rats were subjected to 2 h of middle cerebral artery occlusion
     with the intraluminal filament technique. Plasma AVP levels (means ±
     SD) were significantly elevated at 24 h (42 ± 21 pg/ml), 48 h (50 ±
     28 pg/ml), and 72 h (110 ± 47 pg/ml), and returned to baseline at 96 h
     (22 ± 15 pg/ml) following middle cerebral artery occlusion compared
     with sham-operated controls (14 ± 7 pg/ml). Plasma AVP levels at 72 h
     were significantly attenuated with 7.5% HS (37 ± 8 pg/ml; 360 ± 11
     osmol/l) compared with 0.9% saline (73 ± 6; 292 ± 6 osmol/l), 3% HS
     (66 ± 8 pg/ml; 303 ± 12 osmol/l), or mannitol (74 ± 9 pg/ml; 313
     ± 14 osmol/l) treatment. HS (7.5%) significantly attenuated
     water content in the ipsilateral and contralateral hemispheres compared
     with surgical shams, 0.9% saline, 3% HS, and mannitol treatments
     . Peak plasma AVP levels were not associated with direct
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histopathological injury to the anterior hypothalamus. Attenuation of brain water content with 7.5% HS treatment coincides with attenuated serum AVP levels, and we speculate that this may represent one additional mechanism by which osmotherapy attenuates edema associated with ischemic stroke. Copyright .COPYRGT. 2006 the American Physiological Society.

L22 ANSWER 2 OF 21 MEDLINE on STN DUPLICATE 1
2006196896. PubMed ID: 16357093. Agonist and hypertonic saline-induced trafficking of the NK3-receptors on vasopressin neurons within the paraventricular nucleus of the hypothalamus. Haley Gwendolen E; Flynn Francis W. (Dept. of Zoology and Physiology, Univ. of Wyoming, Laramie, WY 82071, USA.) American journal of physiology. Regulatory, integrative and comparative physiology, (2006 May) Vol. 290, No. 5, pp. R1242-50. Electronic Publication: 2005-12-15. Journal code: 100901230. ISSN: 0363-6119. Pub. country: United States. Language: English.

AB The neurokinin 3 receptor (NK3R) is colocalized with vasopressinergic neurons within the hypothalamic paraventricular nucleus (PVN) and intraventricular injections of NK3R agonists stimulate vasopressin (VP) release. Our objectives were to test the hypotheses that intraventricular injections of the selective NK3R agonist, succinyl-[Asp6, N-Me-Phe8] substance P (senktide), activate NK3R expressed by vasopressinergic neurons within the PVN, and see whether NK3R expressed by vasopressinergic neurons in the PVN are activated by hyperosmolarity. NK3R internalization was used as a marker of receptor activation. Immunohistochemistry revealed that NK3Rs were membrane-bound on VP immunoreactive neurons in control rats. Following senktide injection, there was a significant increase in the appearance of NK3R immunoreactivity within the cytoplasm and a morphological rearrangement of the dendrites, indicating receptor internalization, which was reversible. Furthermore, pretreatment with a selective NK3R antagonist, SB-222200, blocked the senktide-induced VP release and internalization of the NK3R in the PVN. These results show that the trafficking of the NK3R is due to ligand binding the NK3R. In a subsequent experiment, rats were administered intragastric loads of 2 or 0.15 M NaCl, and NK3R immunohistochemistry was used to track activation of the receptor. In contrast to control rats, 2 M NaCl significantly increased plasma VP levels and caused the internalization of the NK3R on VP neurons. Also, NK3R immunoreactivity was located in the nuclei of vasopressinergic neurons after senktide and 2 M NaCl treatment. These results show that hyperosmolarity stimulates the local release of an endogenous ligand in the PVN to bind to and activate NK3R on vasopressinergic neurons.

L22 ANSWER 3 OF 21 EMBASE
2006295070 EMBASE Hyponatremia, hypernatremia: A physiological approach. Offenstadt G.; Das V.. G. Offenstadt, Service de Reanimation Medicale, Hopital Saint-Antoine, 184 rue du Faubourg Saint Antoine, 75012 Paris, France. georges.offenstadt@sat.aphp.fr. Minerva Anestesiologica Vol. 72, No. 6, pp. 353-356 2006.
Refs: 15.
ISSN: 0375-9393. CODEN: MIANAP
Pub. Country: Italy. Language: English. Summary Language: English; Italian.
Entered STN: 20060711. Last Updated on STN: 20060711

AB Natremia belongs to the toolbox of the practicing intensivist. It is an indicator of the hydration status, which is an item that must be continuously monitored in critically ill patients. Hyponatremia is not rare (1% to 2% of hospitalised patients), and hypernatremia is about 10 times less frequent while hypernatremia always indicates hypertonicity, hyponatremia is not equivalent to hypotonicity. Diagnosis depends on the history, clinical examination and basic biochemical data. It should be kept in mind that obtaining urine samples is as important as plasma samples in this respect. The first step consists in confirming that

hyponatremia is hypotonic. The second step is to assess the renal response to hypotonicity. Hypotonic hyponatremia will be considered in association with hypovolemia, euvolemia or hypervolemia. The constitution of a hyperosmolar state requires an inadequate water intake The main goal of the treatment is not to normalize numbers (they must always be checked first), but to treat symptoms. Tolerance must always be appreciated. The mathematical formulas proposed are of interest for a better understanding, but should not be followed strictly.

L22 ANSWER 4 OF 21 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2006224486 EMBASE Agonist and hypertonic saline-induced trafficking of the NK3-receptors on vasopressin neurons within the paraventricular nucleus of the hypothalamus. Haley G.E.; Flynn F.W.. F.W. Flynn, Dept. 3166, Univ. of Wyoming, 1000 E. Univ. Ave., Laramie, WY 82071, United States. flynn@uwyo.edu. American Journal of Physiology - Regulatory Integrative and Comparative Physiology Vol. 290, No. 5, pp. R1242-R1250 2006.

Refs: 41.

ISSN: 0363-6119. E-ISSN: 1522-1490. CODEN: AJPRDO

Pub. Country: United States. Language: English. Summary Language: English.

Entered STN: 20060530. Last Updated on STN: 20060530

AB The neurokinin 3 receptor (NK3R) is colocalized with vasopressinergic neurons within the hypothalamic paraventricular nucleus (PVN) and intraventricular injections of NK3R agonists stimulate vasopressin (VP) release. Our objectives were to test the hypotheses that intraventricular injections of the selective NK3R agonist, succinyl-[Asp(6), N-Me-Phe(8)] substance P (senktide), activate NK3R expressed by vasopressinergic neurons within the PVN, and see whether NK3R expressed by vasopressinergic neurons in the PVN are activated by hyperosmolarity. NK3R internalization was used as a marker of receptor activation. Immunohistochemistry revealed that NK3Rs were membrane-bound on VP immunoreactive neurons in control rats. Following senktide injection, there was a significant increase in the appearance of NK3R immunoreactivity within the cytoplasm and a morphological rearrangement of the dendrites, indicating receptor internalization, which was reversible. Furthermore, pretreatment with a selective NK3R antagonist, SB-222200, blocked the senktide-induced VP release and internalization of the NK3R in the PVN. These results show that the trafficking of the NK3R is due to ligand binding the NK3R. In a subsequent experiment, rats were administered intragastric loads of 2 or 0.15 M NaCl, and NK3R immunohistochemistry was used to track activation of the receptor. In contrast to control rats, 2 M NaCl significantly increased plasma VP levels and caused the internalization of the NK3R on VP neurons. Also, NK3R immunoreactivity was located in the nuclei of vasopressinergic neurons after senktide and 2 M NaCl treatment. These results show that hyperosmolarity stimulates the local release of an endogenous ligand in the PVN to bind to and activate NK3R on vasopressinergic neurons. Copyright .COPYRGT. 2006 the American Physiological Society.

L22 ANSWER 5 OF 21 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2005278040 EMBASE Disorders of water imbalance. Lin M.; Liu S.J.; Lim I.T.. Dr. M. Lin, San Francisco General Hospital Emergency Services, University of California San Francisco, 1001 Potrero Avenue, San Francisco, CA 94110, United States. milin@itsa.ucsf.edu. Emergency Medicine Clinics of North America Vol. 23, No. 3 SPEC. ISS., pp. 749-770 2005.

Refs: 92.

ISSN: 0733-8627. CODEN: EMCAD7

S 0733-8627(05)00002-7. Pub. Country: United States. Language: English. Summary Language: English.

Entered STN: 20050811. Last Updated on STN: 20050811

AB Because of the nonspecific signs and symptoms associated with disorders of water imbalance, emergency physicians must maintain a high index of

suspicion for hyponatremia and hypernatremia, especially in patients at greater risk for these electrolyte disorders. Classifying patients based on their clinical volume status, serum and urine osmolality, and urine sodium concentration helps to identify the cause of the water imbalance and to tailor treatment. Specifically, important laboratory tests to order include a serum and urine sodium concentration, serum and urine osmolality, other electrolyte concentrations, and renal function tests. Choosing the appropriate type of intravenous fluid and calculating the initial fluid resuscitation rate require careful weighing of risks and benefits associated with cellular volume changes in the CNS. Correcting serum sodium concentration too slowly or too rapidly may have devastating consequences. It is essential to monitor serum sodium levels frequently, as often as every 2 to 4 hours initially, during therapy to prevent ODS in hyponatremic patients and cerebral edema in hypernatremic patients. Promising studies involving aquaretics, which are vasopressin receptor antagonists that promote free water excretion, may play a role soon.

L22 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN

2005:698539 Document No. 143:191391 Hyperglycemia does not increase basal hypothalamo-pituitary-adrenal activity in diabetes but it does impair the HPA response to insulin-induced hypoglycemia. Chan, Owen; Inouye, Karen; Akirav, Eitan M.; Park, Edward; Riddell, Michael C.; Matthews, Stephen G.; Vranic, Mladen (Dep. of Physiol., Unit. of Toronto, Toronto, ON, M5S 1A8, Can.). American Journal of Physiology, 289(1, Pt. 2), R235-R246 (English) 2005. CODEN: AJPHAP. ISSN: 0002-9513. Publisher: American Physiological Society.

AB Recently, we established that hypothalamo-pituitary-adrenal (HPA) and counterregulatory responses to insulin-induced hypoglycemia were impaired in uncontrolled streptozotocin (STZ)-diabetic (65 mg/kg) rats and insulin treatment restored most of these responses. In the current study, we used phloridzin to determine whether the restoration of blood glucose alone was sufficient to normalize HPA function in diabetes. Normal, diabetic, insulin-treated, and phloridzin-treated diabetic rats were either killed after 8 days or subjected to a hypoglycemic (40 mg/dL) glucose clamp. Basal: Elevated basal ACTH and corticosterone in STO rats were normalized with insulin but not phloridzin. Increases in hypothalamic corticotrophin-releasing hormone (CRH) and inhibitory hippocampal mineralocorticoid receptor (MR) mRNA with STZ diabetes were not restored with either insulin or phloridzin treatments. Hypoglycemia: In response to hypoglycemia, rises in plasma ACTH and corticosterone were significantly lower in diabetic rats compared with controls. Insulin and phloridzin restored both ACTH and corticosterone responses in diabetic animals. Hypothalamic CRH mRNA and pituitary pro-opiomelanocortin mRNA expression increased following 2 h of hypoglycemia in normal, insulin-treated, and phloridzin-treated diabetic rats but not in untreated diabetic rats. Arginine vasopressin mRNA was unaltered by hypoglycemia in all groups. Interestingly, hypoglycemia decreased hippocampal MR mRNA in control, insulin-, and phloridzin-treated diabetic rats but not uncontrolled diabetic rats, whereas glucocorticoid receptor mRNA was not altered by hypoglycemia. In conclusion, despite elevated basal HPA activity, HPA responses to hypoglycemia were markedly reduced in uncontrolled diabetes. We speculate that defects in the CRH response may be related to a defective MR response. It is intriguing that phloridzin did not restore basal HPA activity but it restored the HPA response to hypoglycemia, suggesting that defects in basal HPA function in diabetes are due to insulin deficiency, but impaired responsiveness to hypoglycemia appears to stem from chronic hyperglycemia.

L22 ANSWER 7 OF 21 MEDLINE on STN

2005069260. PubMed ID: 15698632. Protective effect of dexamethasone on osmotic-induced demyelination in rats. Sugimura Yoshihisa; Murase Takashi; Takefuji Seiko; Hayasaka Shizu; Takagishi Yoshiko; Oiso Yutaka; Murata Yoshiharu. (Department of Teratology and Genetics, Research Institute of Environmental Medicine, Nagoya University, Furo-cho, Chikusa-ku, Nagoya

464-8601, Japan.) Experimental neurology, (2005 Mar) Vol. 192, No. 1, pp. 178-83. Journal code: 0370712. ISSN: 0014-4886. Pub. country: United States. Language: English.

AB Central pontine myelinolysis (CPM) is a serious demyelination disease commonly associated with the rapid correction of hyponatremia. Although its pathogenesis remains unclear, the disruption of the blood-brain barrier (BBB) as a consequence of a rapid increase in serum sodium concentration is considered to play a critical role. Since glucocorticoids are known to influence BBB permeability and prevent its disruption as a result of hypertension or hyperosmolarity, we investigated whether dexamethasone (DEX) could protect against osmotic demyelination in an animal model of CPM. Hyponatremia was induced in rats by liquid diet feeding and dDAVP infusion. Seven days later, the animals' hyponatremia was rapidly corrected by injecting a bolus of hypertonic saline intraperitoneally. Rats subjected to this treatment displayed serious neurological impairment and 77% died within 5 days of rapid correction of their hyponatremia; demyelinative lesions were observed in various brain regions in these animals. On the other hand, rats that were treated with DEX (2 mg/kg, 0 and 6 h after hypertonic saline injection) exhibited minimal neurological impairment and all were alive after 5 days. Demyelinative lesions were rarely seen in the brains of DEX-treated rats. A marked extravasation of endogenous IgG was observed in the demyelinative lesions in the brains of rats that did not receive DEX, indicating disruption of the BBB, but was not observed in DEX-treated rats. Furthermore, Evans blue injection revealed a significant reduction in staining in the brains of DEX-treated rats ($P < 0.05$). These results indicate that early DEX treatment can prevent the BBB disruption that is caused by the rapid correction of hyponatremia and its associative demyelinative changes, and suggest that DEX might be effective in preventing CPM.

L22 ANSWER 8 OF 21 EMBASE

2006177538 EMBASE Hyponatremia in neurological diseases in ICU. Lath R.. Dr. R. Lath, Department of Neurosurgery, Apollo Hospitals, Jubilee Hills, Hyderabad - 500 033, India. rahullath@hotmail.com. Indian Journal of Critical Care Medicine Vol. 9, No. 1, pp. 47-51 1 Jan 2005.
Refs: 19.
ISSN: 0972-5229. Pub. Country: India. Language: English. Summary Language: English.
Entered STN: 20060601. Last Updated on STN: 20060601

AB Hyponatremia is the commonest electrolyte disturbance encountered in the neurological and neurosurgical intensive care units. It can present with signs and symptoms mimicking a neurological disease and can worsen the existing neurological deficits. Hyponatremia in neurological disorders is usually of the hypoosmolar type caused either due to the Syndrome of Inappropriate Secretion of Anti Diuretic Hormone (SIADH) or Cerebral Salt Wasting Syndrome (CSWS). It is important to distinguish between these two disorders, as the treatment of the two differ to a large extent. In SIADH, the fluid intake is restricted, whereas in CSWS the treatment involves fluid and salt replacement.

L22 ANSWER 9 OF 21 EMBASE

2006036347 EMBASE Diabetic hyperosmolarity: A consequence of loss of autonomy. Constans T.. T. Constans, Faculte de Medecine de Tours, Universite Francois-Rabelais, F-37032 Tours Cedex 1, France. t.constans@chu-tours.fr. Diabetes and Metabolism Vol. 31, No. SPEC. ISS. 2, pp. 5S62-5S66 2005.
Refs: 22.
ISSN: 1262-3636. CODEN: DIMEFW
Pub. Country: France. Language: English. Summary Language: English; French.
Entered STN: 20060209. Last Updated on STN: 20060209

AB Diabetic hyperosmolarity is a serious acute metabolic disorder

mainly occurring in the frail elderly subject presenting age-related favoring factors (reduced sensation of thirst, altered endocrine regulation), disease-related favoring factors (cognitive impairment, poor nutritional status and/or loss of autonomy), and a triggering factor, generally infection. Diabetic hyperosmolarity can occur in a previously non-diabetic patient. Intense dehydration dominants the clinical picture. The prognosis depends largely on the underlying chronic disease.

L22 ANSWER 10 OF 21 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2003497606 EMBASE Disorders of body water homeostasis. Verbalis J.G.. Prof. Dr. J.G. Verbalis, Dept. of Medicine and Physiology, Div. of Endocrinol. and Metabolism, Georgetown Univ. School of Medicine, 4000 Reservoir Road NW, Washington, DC 20007, United States. Bailliere's Best Practice and Research in Clinical Endocrinology and Metabolism Vol. 17, No. 4, pp. 471-503 2003.
Refs: 65.
ISSN: 1521-690X. CODEN: BBPMFY
Pub. Country: United Kingdom. Language: English. Summary Language: English.
Entered STN: 20031229. Last Updated on STN: 20031229

AB Disorders of body fluids are among the most commonly encountered problems in the practice of clinical medicine. This is in large part because many different disease states can potentially disrupt the finely balanced mechanisms that control the intake and output of water and solute. It therefore behoves clinicians treating such patients to have a good understanding of the pathophysiology, the differential diagnosis and the management of these disorders. Because body water is the primary determinant of the osmolality of the extracellular fluid, disorders of body water homeostasis can be divided into hypo-osmolar disorders, in which there is an excess of body water relative to body solute, and hyperosmolar disorders, in which there is a deficiency of body water relative to body solute. The classical hyperosmolar disorder is diabetes insipidus (Dl), and the classical hypo-osmolar disorder is the syndrome of inappropriate antidiuretic hormone secretion (SIADH). This chapter first reviews the regulatory mechanisms underlying water and sodium metabolism, the two major determinants of body fluid homeostasis. The major disorders of water metabolism causing hyperosmolality and hypo-osmolality, Dl and SIADH, are then discussed in detail, including the pathogenesis, differential diagnosis and treatment of these disorders.

L22 ANSWER 11 OF 21 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2003120378 EMBASE Management of disorders of water metabolism in patients with pituitary tumors. Verbalis J.G.. Dr. J.G. Verbalis, Div. of Endocrinology/Metabolism, Georgetown Univ. Sch. of Medicine, 4000 Reservoir Road NW, Washington, DC 20007, United States. verbalis@georgetown.edu. Pituitary Vol. 5, No. 2, pp. 119-132 2002.
Refs: 37.
ISSN: 1386-341X. CODEN: PITUF
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20030403. Last Updated on STN: 20030403

AB Disorders of body fluids, notably central diabetes insipidus (CDI) and the syndrome of inappropriate antidiuretic hormone secretion (SIADH), are relatively uncommon as a presenting symptom of sellar and suprasellar masses, but quite common following surgical resection of such lesions. It therefore behooves clinicians treating such patients to have a good understanding of the pathophysiology, the differential diagnosis and the management of these disorders. This review discusses some general issues concerning the pathogenesis, differential diagnosis, clinical manifestations and therapy of hyperosmolar and hypoosmolar syndromes, including CDI and SIADH, and then more specifically addresses the evaluation and treatment of pre- and postoperative disorders of water metabolism in patients with pituitary adenomas.

L22 ANSWER 12 OF 21 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2001343207 EMBASE Effect of chronic treatment with haloperidol on vasopressin release and behavioral changes by osmotic stimulation of the supraoptic nucleus. Hirayama T.; Kita T.; Ogawa Y.; Ohsawa H.; Yamashita M.; Nakashima T.; Kishimoto T.. T. Kishimoto, Department of Psychiatry, Nara Medical University, 840 Shijocho, Kashihara, Nara 634-8522, Japan. toshik@naramed-u.ac.jp. Life Sciences Vol. 69, No. 18, pp. 2147-2156 21 Sep 2001.

Refs: 25.

ISSN: 0024-3205. CODEN: LIFSAK

S 0024-3205(01)01295-4. Pub. Country: United States. Language: English. Summary Language: English.

Entered STN: 20011018. Last Updated on STN: 20011018

AB Chronic treatment with dopamine D(2) blockers in schizophrenic patients has been proposed as one of the causes of polydipsia and water intoxication, but this conclusion is still controversial. To investigate the relationship between dopamine D(2) blockers and these syndromes, we designed a behavioral and neurochemical study using hyperosmotic stimulation in the supraoptic nucleus (SON) by microdialysis after chronic treatment with haloperidol in rats. Animals were injected with haloperidol decanoate (20 mg/kg, i.m.) or sesame oil at 2-week intervals for 8 successive weeks. During the 7th week, water-intake was increased 30-60 min after the hyperosmotic stimulation in both groups, but more so in haloperidol-treated animals compared to that in the control group. Moreover, arginine vasopressin (AVP) was released by the hyperosmotic stimulation in SON, but was not significantly different between groups. In addition, striatal dopamine levels 3-4 days after the microdialysis study showed a significant decrease in the haloperidol-treated animals. These results suggest that chronic treatment with haloperidol enhances water-intake produced by hyperosmotic stimulation in the SON but does not increase AVP levels in dialysates following hyperosmotic stimulation. Thus, these symptoms may be mediated by dopaminergic systems in brain. .COPYRGT. 2001 Elsevier Science Inc. All rights reserved.

L22 ANSWER 13 OF 21 MEDLINE on STN DUPLICATE 2

1999255949. PubMed ID: 10322639. Developmental expression of urine concentration-associated genes and their altered expression in murine infantile-type polycystic kidney disease. Gattone V H 2nd; Maser R L; Tian C; Rosenberg J M; Branden M G. (Department of Anatomy and Cell Biology, University of Kansas Medical Center, Kansas City 66160-7400, USA.. vgattone@kumc.edu) . Developmental genetics, (1999) Vol. 24, No. 3-4, pp. 309-18. Journal code: 7909963. ISSN: 0192-253X. Pub. country: United States. Language: English.

AB Currently, there is little understanding of what factors regulate the development of urine concentrating capability in normal or polycystic kidney. The present study examined the developmental expression of genes associated with urine concentration in developing mice, including C57BL/6J-cpk/cpk mice with autosomal recessive-infantile (AR) polycystic kidney disease (PKD). Concentration of urine requires: 1) medullary collecting ducts (CD) located within a hypertonic interstitium, 2) CD cell expression of functional arginine vasopressin V2 receptors (AVP-V2R), and 3) the presence of appropriate CD water channels (aquaporins, AQP 2 and 3). An increase in urine osmolarity, normally seen between 1 and 3 weeks of age, was absent in cpk cystic mice. Aldose reductase mRNA expression (a gene upregulated by medullary hyperosmolarity) increased in normal mice, but remained low in the cystic kidney, suggesting the absence of a hypertonic medullary interstitium. AVP-V2R, AQP2, and AQP3 mRNA expression normally increase between 7 and 14 days. However, all were dramatically overexpressed even at 7 days of age in the cpk kidney in vivo, but decreased in vitro. Activation of the AVP-V2 receptor stimulates the production of cAMP, a substance known to promote cyst enlargement. To determine if CD cAMP,

generated from increased AVP-V2Rs, was accelerating the PKD, cystic mice and their normal littermates were treated with OPC31260, a relatively specific AVP-V2R antagonist. OPC31260 treatment of cystic mice led to an amelioration of the cystic enlargement and azotemia. Treatment also decreased renal AQP2 mRNA but increased AVP-V2R and AQP3 mRNA expression in vivo. AVP upregulates the expression of AVP-V2R, AQP2, and AQP3 mRNAs in vitro. Renal EGF, known to inhibit AVP-V2R activity, downregulates AVP-V2R mRNA in vitro. Brief in vivo EGF treatment, known to decrease PKD in cpk mice, led to increased expression of AVP-V2R, AQP2, and AQP3 mRNAs at 2 weeks in both normal and cystic mice but no change was evident at 3 weeks of age. In conclusion, the development of urinary concentration ability correlates with the development of an increased medullary osmotic gradient which is diminished in murine ARPKD. However, CD genes associated with this process are overexpressed in vivo but underexpressed in vitro in the cystic kidney. The overexpression and/or overactivity of the AVP-V2R appears to contribute to the progression of PKD since an AVP-V2R antagonist inhibits cystic renal enlargement in the cpk mouse.

L22 ANSWER 14 OF 21 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3

1998188767 EMBASE Upregulation of hypothalamic nitric oxide synthase gene expression in streptozotocin-induced diabetic rats. Serino R.; Ueta Y.; Tokunaga M.; Hara Y.; Nomura M.; Kabashima N.; Shibuya I.; Hattori Y.; Yamashita H.. Dr. H. Yamashita, Department of Physiology, School of Medicine, Univ. of Occupational/Envtl. Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan. Diabetologia Vol. 41, No. 6, pp. 640-648 1998.
Refs: 31.
ISSN: 0012-186X. CODEN: DBTGAJ
Pub. Country: Germany. Language: English. Summary Language: English.
Entered STN: 19980709. Last Updated on STN: 19980709

AB Plasma arginine vasopressin (AVP) is known to be elevated in patients with uncontrolled insulin-dependent diabetes mellitus who have plasma hyperosmolality with hyperglycaemia. Although osmotic stimuli cause an increase in nitric oxide synthase (NOS) activity as well as synthesis of AVP and oxytocin in the paraventricular (PVN) and supraoptic nuclei (SON), it is not known whether NOS activity in the hypothalamus changes in the diabetic patients who have plasma hyperosmolality with hyperglycaemia caused by insulin deficiency. Expression of the neuronal (n) NOS gene in the PVN and SON in streptozotocin (STZ)-induced diabetic rats was investigated by using in situ hybridization histochemistry and NADPH-diaphorase histochemical staining. Four weeks after intraperitoneal (i. p.) administration of STZ, male Wistar rats developed hyperglycaemia and plasma hyperosmolality. The expression of nNOS gene and NADPH-diaphorase staining in the PVN and SON remarkably increased in STZ-induced diabetic rats compared to control rats. Three weeks after administration of STZ, the diabetic rats were subcutaneously treated with insulin for 1 week, which resulted in significant suppression of the induction of nNOS, AVP and oxytocin gene expression in the PVN and SON. Furthermore, the induction of nNOS gene expression in the PVN and SON was suppressed in STZ-induced diabetic rats treated with phlorizin and diet to normalize hyperglycaemia without insulin treatment. These results suggest that upregulation of nNOS gene expression as well as AVP and oxytocin gene expression in the PVN and SON in STZ-induced diabetic rats may be associated with hyperglycaemia and plasma hyperosmolality.

L22 ANSWER 15 OF 21 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

1998309509 EMBASE Hypertonic saline resuscitation. Rocha e Silva M.. Dr. M. Rocha e Silva, Instituto del Corazon, Av. Eneas de Carvalho Aguiar 44, Sao Paulo, SP, CEP 05403-000, Brazil. mrsilva@incor.usp.br. Medicina Vol. 58, No. 4, pp. 393-402 1998.
Refs: 186.
ISSN: 0025-7680. CODEN: MEDCAD

Pub. Country: Argentina. Language: English. Summary Language: English; Spanish.
Entered STN: 19981009. Last Updated on STN: 19981009

AB Treatment of severe hemorrhage offers few theoretical problems, but in practice, severe blood loss usually occurs out of hospital, often in more or less inaccessible scenarios. Controversy rages over ideal fluid, ideal volume, and minimum O2 carrying capacity, but all agree that pre-hospital, isotonic resuscitation is unfeasible. The effects of highly hypertonic 7.5% NaCl (HS) was first described in 1980, when we showed that it induced immediate and long lasting hemodynamic restoration. The addition of 6% dextran-70 to (HSD) significantly enhances the duration and intensity of volume expansion, with no loss of hemodynamic effects. HS/HSD restores cardiac output, arterial pressure, base excess and oxygen availability, induce pre-capillary vasodilation, moderate hyperosmolarity and hypernatremia, reversal of high glucose and lactate. It interferes with endocrine secretions when administered to animals in hemorrhagic hypotension. HS acts through transient plasma volume expansion, positive inotropic effect on cardiac contractility, precapillary vasodilation through a direct action on vascular smooth muscle. Expansion of circulating volume is part of the mechanism, the extra volume coming from the intracellular compartment fluid, especially from endothelial and red blood cells, which facilitate microcirculatory flow. The new field of interactions of hypertonicity with the immune mechanisms may provide insight into the long lasting effects of hypertonic solutions. Randomized double blind prospective studies on the effects of HS, or HSD, used as first treatment of shock show that both are safe and free from collateral, toxic effects. These studies show an early significant rise in arterial blood pressure and a non-significant trend towards higher levels of survival. HSD administration to patients about to undergo cardiopulmonary bypass for cardiac surgery results in higher cardiac output before, and immediately following cardiopulmonary bypass, as well as zero fluid balance.

L22 ANSWER 16 OF 21 MEDLINE on STN DUPLICATE 4
1998070398. PubMed ID: 9405432. Hyperosmolarity-induced gene stimulation is mediated by the negative calcium responsive element. Okazaki T; Ishikawa T; Nishimori S; Igarashi T; Hata K; Fujita T. (Endocrine Genetics and Hypertension Unit, 4th Department of Internal Medicine, University of Tokyo School of Medicine, Bunkyo-ku, Tokyo 112, Japan.. okbgeni-tky@umin.u-tokyo.ac) . The Journal of biological chemistry, (1997 Dec 19) Vol. 272, No. 51, pp. 32274-9. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The negative calcium responsive elements of the parathyroid hormone gene bind to a specific set of nuclear proteins in an extracellular calcium (Ca2+e)-dependent manner. We have found that one of the negative calcium responsive elements, named oligo B, is found in the 5'-flanking region of such vasoactive genes as the vasopressin and atrial natriuretic polypeptide genes. Furthermore, the oligo B-like sequence in the former gene is conserved throughout evolution. Because expression of some of these vasoactive genes is altered by external stimuli which change cell volume, we examined whether oligo B is involved in gene regulation by hyperosmolarity. Here, we demonstrate that the binding between oligo B and its binding nuclear proteins including a redox factor 1 was reduced by hyperosmolarity generated by sodium chloride but not by urea. Such attenuated binding was reversed by dephosphorylating nuclear proteins by a potato acid phosphatase, suggesting that NaCl treatment elicited phosphorylation of these nuclear proteins to weaken their binding activity to oligo B. Furthermore, these nuclear events led to hyperosmolarity-mediated transcriptional stimulation of the genes bearing this DNA element in the cultured cells.

L22 ANSWER 17 OF 21 EMBASE DUPLICATE 5
88027910 EMBASE Document No.: 1988027910. Chronic intracerebroventricular morphine and lactation in rats: Dependence and tolerance in relation to

oxytocin neurones. Rayner V.C.; Robinson I.C.A.F.; Russell J.A.. Department of Physiology, University Medical School, Edinburgh, EH8 9AG, United Kingdom. Journal of Physiology Vol. 396, pp. 319-347 1988. ISSN: 0022-3751. CODEN: JPHYA7
Pub. Country: United Kingdom. Language: English. Summary Language: English.
Entered STN: 911211. Last Updated on STN: 911211

AB 1. Acutely, opioids inhibit oxytocin secretion. To study the responses of oxytocin neurones during chronic opioid exposure, forty-five lactating rats were infused continuously from a subcutaneous osmotically driven mini-pump via a lateral cerebral ventricle with morphine sulphate solution from day 2 post-partum for 5-7 days; the infusion rate was increased 2- or 2.5-fold each 40 h from 10 μg/h initially up to 50 μg/h; controls were infused with vehicle (1 μl/h, twenty-eight rats) or were untreated (eight rats). 2. Maternal behaviour was disrupted in 27% of the morphine-treated rats; in rats that remained maternal morphine did not affect body weight or water intake but increased rectal temperature by 0.82±0.14°C (mean±S.E.M.) across the first 4 days. 3. Weight gain of the litters of maternal morphine-treated rats was reduced by 32% during 7 days, predominantly in the first day of treatment when milk transfer was also reduced. Observation of pup behaviour during suckling showed decreased frequency of milk ejections on only the second day of morphine treatment. Plasma concentration of prolactin after 6 days was similar in maternal morphine-treated and control rats, but reduced by 90% in non-maternal morphine-treated rats, indicating normal control of prolactin secretion by suckling in morphine-treated rats. 4. Oxytocin and vasopressin contents, measured by radioimmunoassay, in the supraoptic and paraventricular nuclei and in the neurohypophysis were similar between fourteen maternal morphine-treated, twelve vehicle-treated and eight untreated lactating rats; thus exposure to morphine did not involve increased production and storage of oxytocin. 5. Distribution of [3H]morphine infused intracerebroventricularly into six virgin female rats for 6 days was measured by scintillation counting of tissue extracts. Morphine concentration in the hypothalamus and neurohypophysis was 2.7 and 12.8 μg/g, respectively, and in blood plasma 0.75 μg/g. Tolerance was not due to failure of morphine infusion. In addition, naloxone (5 mg/kg S.C.) provoked typical withdrawal reactions ('wet dog' shakes, defaecation, burrowing) in lactating rats infused with morphine for 5 days. 6. Pups were suckled onto seven maternal morphine-infused and five vehicle-infused rats anaesthetized with urethane for recording of intramammary and arterial blood pressures after treatment for 5 days. The incidence and pattern of milk ejections, and mammary gland sensitivity to oxytocin were similar in the two groups. Tolerance to the inhibition of suckling-induced oxytocin secretion by intracerebroventricular (I.C.V.) morphine did not extend to acute intravenous morphine (2.5 or 5 mg/kg). 7. In fourteen out of fifteen morphine-infused rats under urethane anaesthesia, intravenous naloxone HCl (5 mg/kg) quickly provoked a large, fluctuating increase in intramammary pressure lasting 41.5±15 min (mean±S.D.); this excitation of presumptive oxytocin secretion was independent of suckling and was not seen in twelve vehicle-infused rats. Carbachol I.C.V. (0.2 μg) produced a similar excitation of oxytocin release in both groups of rats. Naloxone did not reveal or produce stimulation of oxytocin secretion by hypotension, hypernatraemia or hyperosmolarity of extracellular fluid. 8. It is concluded that chronic I.C.V. morphine infusion leads to the development of both tolerance and dependence in the mechanisms that lead to oxytocin secretion, i.e. in an identifiable peptidergic neurosecretory system. This provides a new model for the study of the processes involved in the acute and chronic actions of opioids on neurones.

L22 ANSWER 18 OF 21 EMBASE

86058034 EMBASE Document No.: 1986058034. [The principal endocrine paraneoplastic syndromes accompanying lung cancer. Pathophysiologic-

clinical correlations and therapeutic approaches]. LE PRINCIPALI SINDROMI PARANEOPLASTICHE ENDOCRINE NEL CANCRO POLMONARE. CORRELAZIONI FISIOPATOLOGICO-CLINICHE ED APPROCCIO TERAPEUTICO. Di Lollo F.; Cerinic M.M.. Divisione Medica, USL N. 10, Ospedale di Careggi, Istituto di Clinica Medica II dell'Universita di Firenze, Firenze, Italy. Clinica Terapeutica Vol. 115, No. 4, pp. 283-295 1985.
CODEN: CLTEA4
Pub. Country: Italy. Language: Italian. Summary Language: English.
Entered STN: 911210. Last Updated on STN: 911210

AB Discussion is limited to the most frequently observed paraneoplastic syndromes accompanying lung cancer, among which inappropriate ACTH secretion is the most frequent one. From the clinical point of view certain aspects of this syndrome differ from Cushing syndrome in as much as it is characterized by lack of response of urinary 17 KS to tests of stimulation and inhibition, by high levels of circulating ACTH and failure of dexamethasone administration to influence cortisol blood level. Therapeutic intervention is aimed above all at the speedy correction of K+ depletion. The paraneoplastic syndrome due to inadequate ADH secretion is characterized by fluid retention (increased circulating blood volume), hyponatremia and hypochloremia (plasma hyperosmolarity), oliguria and absence of heart, kidney and adrenal disorders. Therapeutic measures consist in limiting fluid intake, administering cortisone, and adding NaCl to slow infusion only in cases with signs of cerebral impairment. Pseudohyperparathyroidism caused by the secretion of PTH-similar substances is accompanied by high urinary hydroxyproline excretion and disorders of phosphorus and calcium household: hypercalcemia, increased alkaline phosphatase, increased calciuria and phosphaturia. Hypercalcemia requires early treatment using calcitonin in order to reduce circulating Ca++ (blockage of osteoclasts), corticosteroids (block of Ca++ absorption in the intestine), furosemide (increased urinary Ca++ excretion). In addition, fluid and salt depletion and the metabolic deviations favoring calcium ionization must be corrected.

L22 ANSWER 19 OF 21 MEDLINE on STN DUPLICATE 6
82132708. PubMed ID: 7036730. Neurogenic disorders of osmoregulation. Robertson G L; Aycinena P; Zerbe R L. The American journal of medicine, (1982 Feb) Vol. 72, No. 2, pp. 339-53. Ref: 110. Journal code: 0267200. ISSN: 0002-9343. Pub. country: United States. Language: English.

AB The osmolality of body fluids is normally maintained within a narrow range. This constancy is achieved largely via hypothalamic osmo-receptors that regulate thirst and arginine vasopressin, the antidiuretic hormone (ADH). Anything that interferes with the full expression of either osmoregulatory function exposes the patient to the hazards of abnormal increases or decreases in plasma osmolality. Hyposmolality is almost always due to a defect in water excretion. Increased intake may contribute to the problem but is rarely, if ever, a sufficient cause. Impaired water excretion can be due to a primary defect in the osmoregulation of ADH (inappropriate antidiuresis) or secondary to nonosmotic stimuli like hypovolemia or nausea. The two types differ in clinical presentation and treatment. Resetting of the ADH osmostat is commonly associated with resetting of the thirst osmostat. Hyperosmolarity is almost always due to deficient water intake. Excessive excretion may contribute to the problem but is never a sufficient cause. Impaired water intake can result from a defect in either the osmoregulation of thirst of the necessary motor responses. Thirst may be deficient because of primary osmoreceptor damage as in the syndrome of adipsic hypernatremia or secondary to nonosmotic influences on the set of the system. They are distinguishable by the clinical presentation as well as the type of ADH defects with which they are associated. So-called essential hypernatremia due to primary resetting of the osmostat has been postulated, but unambiguous evidence for such an entity has not yet been reported.

L22 ANSWER 20 OF 21 EMBASE

reserved on STN
79145974 EMBASE Document No.: 1979145974. [Hypothalamic hyperosmolarity in childhood]. HYPOTHALAMISCH BEDINGTE STORUNGEN DER OSMOREGULATION IM KINDESALTER. Andler W.; Roosen K.; Reinhardt V.. Klinderklin., Univ., GHS Essen, Germany. Neurochirurgia Vol. 22, No. 2, pp. 56-68 1979.
CODEN: NURABV
Pub. Country: Germany. Language: German. Summary Language: English.
AB Hypothalamic lesions occasionally lead to excessive hypernatraemia and hyperosmolarity which cannot be explained by defective ADH secretion alone. As osmoregulation is a complex system the clinical features differ widely from one patient to another. In general central dysregulation of osmolarity is due to diffuse hypothalamic lesions, e.g. inflammatory infiltration by histiocytosis X or by large suprasellar tumours. We report on a ten-year-old girl suffering from a suprasellar spongioblastoma and a twelve-year-old girl, who had been operated on for a large craniopharyngioma. Polyuria and polydipsia were not present. Whereas one patient presented hypernatraemic crises and showed normal osmolarity at the intervals, the other patient suffered from sustained hypernatraemia and hyperosmolarity. In the first patient water loading led promptly to clinical and laboratory normalisation. In the other case water loading failed to decrease hyperosmolarity but led to oedema. In the first patient hypernatraemic crises were combined with decreased serum potassium levels and elevated urinary aldosterone excretion. Therefore acute and long-term trials of spironolactone treatment were successful. Exogenous ADH-derivates failed to normalize hyperosmolarity. In the other patient, however, DDAVP decreased the serum sodium level even with small doses.

L22 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
1966:21723 Document No. 64:21723 Original Reference No. 64:4041h,4042a-c
The origin of antidiuretic substances and an explanation of the hypernatriuria in the Schwartz-Bartter syndrome. Lebacq, E.; Delaere, J. (Univ. Louvain, Belg.). Annales d'Endocrinologie, 26(3), 375-82 (French) 1965. CODEN: ANENAG. ISSN: 0003-4266.
AB Two patients showed the metabolic disturbances of the Schwartz-Bartter syndrome (Schwartz, et al., Am. J. Med. 23, 529-42(1957)): hypernatriuresis and urine hyperosmolarity, despite hyponatremia and low plasma osmolarity. The 1st patient had a duodenal cancer (118 g.), and the natriuria was not modified by the administration of aldosterone (200 γ/day for 2 days). The condition was not modified by the oral administration of 100 ml. of 50% EtOH, nor by a perfusion of 120 milliunits of vasopressin over 1 hr. Exts. of urine and of the duodenal tumor were tested for arginine vasopressin. A 24-hr. urine sample contained 1200 milliunits of vasopressin, and the tumor (11 g. of Me2CO powder) contained 8 milliunits/mg. of powder. The antidiuretic activity of the exts. disappeared on treatment with thioglycolate. The 2nd patient had a cancer of the bronchus, and whereas restriction of H2O intake ameliorated the condition, treatment with cortisone, prednisone, 95% EtOH, diphenylhydantoin, hygroton, or 20% mannitol had no effect. The natriuresis was due mainly to a disturbed proximal reabsorption of Na+, and not to an inhibition of aldosterone secretion or an increased glomerular filtration rate in these patients. 34 references.

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L23 36476 (OGATA E?/AU OR ONUMA E?/AU OR TSUNENARI T?/AU OR SAITO H?/AU OR AZUMA Y?/AU)

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L25 ANSWER 1 OF 8 MEDLINE on STN DUPLICATE 1
2005285209. PubMed ID: 15930357. Increased renal calcium reabsorption by parathyroid hormone-related protein is a causative factor in the development of humoral hypercalcemia of malignancy refractory to osteoclastic bone resorption inhibitors. Onuma Etsuro; Azuma Yumiko; Saito Hidemi; Tsunenari Toshiaki ; Watanabe Toshihiko; Hirabayashi Manabu; Sato Koh; Yamada-Okabe Hisafumi; Ogata Etsuro. (Pharmaceutical Department IV, Chugai Research Laboratories, Chugai Pharmaceutical, Co., Ltd., Kanagawa, Japan.) Clinical cancer research : an official journal of the American Association for Cancer Research, (2005 Jun 1) Vol. 11, No. 11, pp. 4198-203. Journal code: 9502500. ISSN: 1078-0432. Pub. country: United States. Language: English.

AB PURPOSE: Bisphosphonate and calcitonin lower blood calcium in humoral hypercalcemia of malignancy (HHM) by suppressing osteoclastic bone resorption, but repeated administration of these drugs often leads to relapse. In this study, we examined the roles of parathyroid hormone-related protein (PTHrP) in the development of bisphosphonate- and calcitonin-refractory HHM. EXPERIMENTAL DESIGN: Nude rats bearing the LC-6 JCK tumor xenograft (LC-6 rats) exhibited high bone turnover and HHM. Repeated administration of alendronate induced a sustained suppression of the bone resorption, but it caused only early and transient reduction of the blood calcium levels, leading to unresponsiveness to the drug. Because high blood levels of PTHrP were detected in the LC-6 rats, those that developed alendronate-refractory HHM were treated with an anti-PTHrP antibody. RESULTS: Administration of anti-PTHrP antibody to animals that received repeated administration of alendronate, thereby developing alendronate-refractory HHM, resulted in an increase in fractional excretion of calcium and a marked decrease of blood calcium level. Drug-refractory HHM was also observed in animals that received another osteoclast inhibitor, an eel calcitonin analogue elcatonin. The blood calcium level decreased after the initial administration of elcatonin, but it eventually became elevated during repeated administration. Administration of the anti-PTHrP antibody, but not of alendronate, effectively reduced the blood calcium of the animals that developed elcatonin-refractory HHM. CONCLUSION: High levels of circulating PTHrP and the resulting augmentation of renal calcium reabsorption is one of the major causes of the emergence of osteoclast inhibitor-refractory HHM. Thus, blockage of PTHrP functions by a neutralizing antibody against PTHrP would benefit patients who develop bisphosphonate- or calcitonin-refractory HHM.

L25 ANSWER 2 OF 8 MEDLINE on STN DUPLICATE 2
2005311286. PubMed ID: 15800941. Parathyroid hormone-related protein (PTHrP) as a causative factor of cancer-associated wasting: possible involvement of PTHrP in the repression of locomotor activity in rats bearing human tumor xenografts. Onuma Etsuro; Tsunenari Toshiaki; Saito Hidemi; Sato Koh; Yamada-Okabe Hisafumi; Ogata Etsuro. (Pharmaceutical Research Department IV, Kamakura Research Laboratories, Chugai Pharmaceutical Co., Kanagawa, Japan.) International journal of cancer. Journal international du cancer, (2005 Sep 1) Vol. 116, No. 3, pp. 471-8. Journal code: 0042124. ISSN: 0020-7136. Pub. country: United States. Language: English.

AB Nude rats bearing the LC-6-JCK human lung cancer xenograft displayed cancer-associated wasting syndrome in addition to humoral hypercalcemia of malignancy. In these rats, not only PTHrP but also several other human proinflammatory cytokines, such as IL-6, leukemia-inducing factor, IL-8, IL-5 and IL-11, were secreted to the bloodstream. Proinflammatory cytokines induce acute-phase reactions, as evidenced by a decrease of serum albumin and an increase in alpha1-acid glycoprotein. Tumor resection abolished the production of proinflammatory cytokines and

improved acute-phase reactions, whereas anti-PTHrP antibody affected neither proinflammatory cytokine production nor acute-phase reactions. Nevertheless, tumor resection and administration of anti-PTHrP antibody similarly and markedly attenuated not only hypercalcemia but also loss of fat, muscle and body weight. Body weight gain by anti-PTHrP antibody was associated with increased food consumption; increased body weight from anti-PTHrP antibody was observed when animals were freely fed but not when they were given the same feeding as those that received only vehicle. Furthermore, nude rats bearing LC-6-JCK showed reduced locomotor activity, less eating and drinking and low blood phosphorus; and anti-PTHrP antibody restored them. Although alendronate, a bisphosphonate drug, decreased blood calcium, it affected neither locomotor activity nor serum phosphorus level. These results indicate that PTHrP represses physical activity and energy metabolism independently of hypercalcemia and proinflammatory cytokine actions and that deregulation of such physiologic activities and functions by PTHrP is at least in part involved in PTHrP-induced wasting syndrome.

L25 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 3

2003534792. PubMed ID: 14613038. Treatment of malignancy-associated hypercalcemia and cachexia with humanized anti-parathyroid hormone-related protein antibody. Sato Koh; Onuma Etsuro; Yocum Richard C; Ogata Etsuro. (Department of International Coordination, Chugai Pharmaceutical Co, Ltd, Skizuuoka, Japan.) Seminars in oncology, (2003 Oct) Vol. 30, No. 5 Suppl 16, pp. 167-73. Ref: 11. Journal code: 0420432. ISSN: 0093-7754. Pub. country: United States. Language: English.

AB Parathyroid hormone-related protein (PTHrP) plays a central role in humoral hypercalcemia of malignancy (HHM), which is one of the most frequent paraneoplastic syndromes. PTHrP produced by the tumor acts through a common PTH/PTHrP receptor to promote bone resorption, inhibit calcium excretion from the kidney, and induce hypercalcemia. Patients with HHM often develop cachexia associated with typical symptoms such as anorexia, malaise, nausea, constipation, polyuria, polydipsia, and confusion. The etiology of the cachexia is not fully understood but is thought to be caused by hypercalcemia and various cytokines such as interleukin-6, tumor necrosis factor-alpha, leukemia inhibitory factor, and others. In this study, we investigated the role of PTHrP in hypercalcemia and cachexia in HHM by using humanized anti-PTHrP antibody. A mouse monoclonal antibody that binds to PTHrP amino acid sequence 1-34 and inhibits PTHrP function has been humanized to create a specific and potent agent for the treatment of patients with HHM. The mouse monoclonal antibody has been shown to have antihypercalcemic activity against nude mice bearing human tumors. Because a mouse antibody is highly immunogenic in human patients, the complementarity-determining regions from the mouse antibody were grafted into a human antibody. The resulting humanized antibody specifically recognizes PTHrP(1-34) and neutralizes PTHrP functions in vitro and in vivo. The humanized anti-PTHrP antibody was administered intravenously to HHM model animals bearing tumors such as LC-6 human lung carcinoma. These animals showed symptoms similar to those of patients with HHM (eg, hypercalcemia and cachexia). The humanized anti-PTHrP antibody-treated animals responded with normalization of blood ionized calcium level through an improvement of bone metabolism and calcium excretion. Moreover, the treated animals also showed an improvement in body weight, ultromotivity, metabolic alkalosis, food consumption, water intake, serum phosphorus, and renal function. Consequently, the humanized antibody-treated animals experienced complete resolution of hypercalcemia and cachexia. These results suggest that the humanized antibody would be an effective and beneficial agent for patients with HHM, and that PTHrP is a major pathogenetic factor of hypercalcemia and cachexia in patients with HHM.

L25 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2002:888597 Document No. 138:3671 Angiogenesis inhibitors that block binding

of PTH-related peptide to its receptor for use as antitumor agents. Saito, Hidemi; Tsunenari, Toshiaki; Onuma, Etsuro; Kato, Atsuhiko; Suzuki, Masami (Chugai Seiyaku Kabushiki Kaisha, Japan). PCT Int. Appl. WO 2002092133 A1 20021121, 110 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2002-JP4586 20020510. PRIORITY: JP 2001-140659 20010510.

AB It is found out that angiogenesis can be inhibited by a substance which inhibits the binding of a parathyroid hormone-associated peptide (e.g. PTHrP) to its receptor. The angiogenesis inhibitors can be anti-PTHrP antibodies, antibody fragments, humanized or chimeric antibodies, PTH receptor antagonists, or antisense oligonucleotides specific to PTHrP. These modified anti-PTHrP antibodies and PTH receptor antagonists are useful as antitumor agents and bone metastasis inhibitors.

L25 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2001:31355 Document No. 134:99582 Remedies for drug-resistant hypercalcemia. Saito, Hidemi; Tsunenari, Toshiaki; Onuma, Etsuro (Chugai Seiyaku Kabushiki Kaisha, Japan). PCT Int. Appl. WO 2001002012 A1 20010111, 118 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP4523 20000706. PRIORITY: JP 1999-192270 19990706.

AB Remedies for drug-resistant hypercalcemia which contain as the active ingredient a substance inhibiting the binding of a parathyroid hormone-related peptide to its receptor. Therapeutics for drug-resistant hypercalcemia include bone resorption inhibitor (e.g. bisphosphates and/or calcitonin), calcium excretion promoter, intestinal calcium absorption inhibitor, or loop diuretic. The PTHrP and receptor-binding inhibitors are PTHrP receptor antagonist such as anti-PTHrP antibodies or fragments or chimeric antibodies.

L25 ANSWER 6 OF 8 MEDLINE on STN DUPLICATE 4

2000354698. PubMed ID: 10898333. Parathyroid hormone-related protein as a potential target of therapy for cancer-associated morbidity. Ogata E. (Japanese Foundation for Cancer Research, Tokyo.) Cancer, (2000 Jun 15) Vol. 88, No. 12 Suppl, pp. 2909-11. Journal code: 0374236. ISSN: 0008-543X. Pub. country: United States. Language: English.

AB BACKGROUND: Proinflammatory cytokines are involved in the genesis of cancer-associated cachexia. Parathyroid hormone-related protein (PTHrP) is the causative agent in humoral hypercalcemia of malignancy (HHM) and is frequently secreted from various kinds of solid tumors as well as from adult T-cell leukemia/lymphoma. PTHrP, like PTH, acts on PTH receptor type 1 (PTH1R). Activation of PTH1R may lead to stimulation of secretion of proinflammatory cytokines.. It is expected, therefore, that PTHrP constitutes a key factor in the activation of the proinflammatory and cachectogenic cytokine network and consequently in the development of cachexia in patients with cancer. METHODS: Two groups of cancer-bearing patients of similar clinical backgrounds were enrolled. Plasma concentrations of PTHrP and cytokines were measured with immunoradiometric assay and radioimmunoassay, respectively. Cancer tissues from patients with HHM were transplanted into nude mice or nude rats. The effects of humanized antihuman PTHrP antibody were examined.

RESULTS: In clinical studies, Group B patients (with elevated plasma PTHrP), compared with Group A patients (with normal plasma PTHrP), tended to exhibit higher plasma levels of tumor necrosis factor (TNF)-alpha (P = 0.13), interleukin (IL)-5 (P = 0.08), and IL-8 (P = 0.08), and had significantly higher levels of IL-6 (P = < or =0.01). The levels of TNF-alpha and IL-6 correlated with those of PTHrP. In animal studies, the antibody caused a prompt and sustained decline in serum calcium. This response was accompanied by improvements in food intake, drinking, body weight gain, and general behavior. It also ameliorated the suppression of serum ADH. When those effects were compared with those induced either by bisphosphonate or calcitonin, it turned out that not all of the beneficial effects of the antibody were directly correlated with the depression of blood calcium. CONCLUSIONS: PTHrP is a promising molecular target for the development of a novel mode of treatment for patients with cancer-associated morbidity.

L25 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2000:244979 Document No.: PREV200000244979. The possibility of utilizing humanized anti-PTHrP antibody as an anti-HHM/cachexia agent. Onuma, Etsuro [Reprint author]; Saito, H.; Azuma, Y.; Shimizu, N.; Tsunenari, T.; Sato, K.; Ogata, E.. Chugai Pharmaceutical, Shizuoka, Japan. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 287. print.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000.
ISSN: 0197-016X. Language: English.

L25 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2000:534320 Document No.: PREV200000534320. PTHrP: The most potent cachectogenic factor shown in an animal model. Ogata, E. [Reprint author]; Takahashi, S. [Reprint author]; Onuma, E.; Sato, K.. Cancer Institute Hospital, Tokyo, Japan. Bone (New York), (October, 2000) Vol. 27, No. 4 Supplement, pp. 21S. print.
Meeting Info.: 2000 International Bone and Hormone Meeting. Hamilton Island, Great Barrier Reef, Queensland, Australia. November 04-07, 2000. International Bone and Mineral Society.
CODEN: BONEDL. ISSN: 8756-3282. Language: English.

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=> s l23 and treatment
L26       4243 L23 AND TREATMENT

=> s l26 and vasopressin level
L27          0 L26 AND VASOPRESSIN LEVEL

=> s l26 and vesopressin
L28          0 L26 AND VESOPRESSIN

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L29          0 L26 AND HYPEROSMOLARITY

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L30         20 L26 AND ANTI-PTHRP

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PROCESSING COMPLETED FOR L30
L31           6 DUP REMOVE L30 (14 DUPLICATES REMOVED)

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L31 ANSWER 1 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
2005255152 EMBASE Increased renal calcium reabsorption by parathyroid hormone-related protein is a causative factor in the development of

humoral hypercalcemia of malignancy refractory to osteoclastic bone resorption inhibitors. Onuma E.; Azuma Y.; Saito H.; Tsunenari T.; Watanabe T.; Hirabayashi M.; Sato K.; Yamada-Okabe H.; Ogata E.. H. Yamada-Okabe, Pharmaceutical Research Department IV, Kamakura Research Laboratories, Chugai Pharmaceutical, Co., Ltd., 200 Kajiwara, Kamakura, 247-8530 Kanagawa, Japan. okabehsf@chugai-pharm.co.jp. Clinical Cancer Research Vol. 11, No. 11, pp. 4198-4203 1 Jun 2005.
Refs: 18.
ISSN: 1078-0432. CODEN: CCREF4
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20050707. Last Updated on STN: 20050707

AB Purpose: Bisphosphonate and calcitonin lower blood calcium in humoral hypercalcemia of malignancy (HHM) by suppressing osteoclastic bone resorption, but repeated administration of these drugs often leads to relapse. In this study, we examined the roles of parathyroid hormone-related protein (PTHrP) in the development of bisphosphonate- and calcitonin-refractory HHM. Experimental Design: Nude rats bearing the LC-6 JCK tumor xenograft (LC-6 rats) exhibited high bone turnover and HHM. Repeated administration of alendronate induced a sustained suppression of the bone resorption, but it caused only early and transient reduction of the blood calcium levels, leading to unresponsiveness to the drug. Because high blood levels of PTHrP were detected in the LC-6 rats, those that developed alendronate-refractory HHM were treated with an anti-PTHrP antibody. Results: Administration of anti-PTHrP antibody to animals that received repeated administration of alendronate, thereby developing alendronate-refractory HHM, resulted in an increase in fractional excretion of calcium and a marked decrease of blood calcium level. Drug-refractory HHM was also observed in animals that received another osteoclast inhibitor, an eel calcitonin analogue elcatonin. The blood calcium level decreased after the initial administration of elcatonin, but it eventually became elevated during repeated administration. Administration of the anti-PTHrP antibody, but not of alendronate, effectively reduced the blood calcium of the animals that developed elcatonin-refractory HHM. Conclusion: High levels of circulating PTHrP and the resulting augmentation of renal calcium reabsorption is one of the major causes of the emergence of osteoclast inhibitor-refractory HHM. Thus, blockage of PTHrP functions by a neutralizing antibody against PTHrP would benefit patients who develop bisphosphonate- or calcitonin-refractory HHM.

L31 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
2005628438. PubMed ID: 16309168. Humanized monoclonal antibody against parathyroid hormone-related protein suppresses osteolytic bone metastasis of human breast cancer cells derived from MDA-MB-231. Saito Hidemi ; Tsunenari Toshiaki; Onuma Etsuro; Sato Koh; Ogata Etsuro; Yamada-Okabe Hisafumi. (Pharmaceutical Research Department III, Kamakura Research Laboratories, Chugai Pharmaceutical Co., Ltd., Kamakura, Kanagawa 247-8530, Japan.) Anticancer research, (2005 Nov-Dec) Vol. 25, No. 6B, pp. 3817-23. Journal code: 8102988. ISSN: 0250-7005. Pub. country: Greece. Language: English.

AB BACKGROUND: Parathyroid hormone-related protein (PTHrP) has been implicated in bone metastasis. However, the effects on bone metastasis of blocking the PTHrP function have not been tested in the clinic. Here, the effects of a humanized anti-PTHrP monoclonal antibody (mAb) on bone metastasis in a human xenograft model are shown. MATERIALS AND METHODS: Subline MDA-5a, with high bone metastatic activity, was established from the human breast cancer cell line MDA-MB-231. Mice were injected with MDA-5a and an anti-PTHrP monoclonal antibody (mAb) raised against human PTHrP (1-34); bone metastasis was evaluated by X-ray photography. RESULTS: MDA-5a produced elevated levels of PTHrP, Interleukin 8 (IL-8), IL-6 and matrix metalloproteinase 1 (MMP-1) and frequently metastasized to the bone. Administration of the humanized anti-PTHrP mAb significantly suppressed

osteolytic bone metastasis of MDA-5a and caused osteogenesis at the sites of metastasis. CONCLUSION: The humanized anti-PTHrP mAb was effective against bone metastasis by inducing osteogenesis and, therefore, will provide a new treatment option for bone metastasis in breast cancer.

L31 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 2

2004546213. PubMed ID: 15517871. Generation of a humanized monoclonal antibody against human parathyroid hormone-related protein and its efficacy against humoral hypercalcemia of malignancy. Onuma Etsuro ; Sato Koh; Saito Hidemi; Tsunenari Toshiaki; Ishii Kimie; Esaki Keiko; Yabuta Naohiro; Wakahara Yuji; Yamada-Okabe Hisafumi; Ogata Etsuro. (Chugai Research Laboratories, Chugai Pharmaceutical Co. Ltd., 200 Kajiwara, Kamakura, Kanagawa, Japan.) Anticancer research, (2004 Sep-Oct) Vol. 24, No. 5A, pp. 2665-73. Journal code: 8102988. ISSN: 0250-7005. Pub. country: Greece. Language: English.

AB A humanized monoclonal antibody against parathyroid hormone-related protein (PTHrP) was generated from the mouse monoclonal antibody raised against the peptide corresponding to the N-terminal 34 amino acids of the human PTHrP [(PTHrP(1-34)]. The humanized antibody interacted with the PTHrP(1-34) with a kD value of 1.90 x 10(-10) M, and the epitope resides between the amino acids 20 and 30 of the PTHrP. PTHrP(1-34) significantly increased the intracellular cAMP levels in the rat osteosarcoma cells that expressed PTHR1, and the 5 microg/mL or higher concentrations of the humanized antibody almost completely blocked the PTHrP-induced cAMP production even in the presence of 2 microg/mL PTHrP(1-34), demonstrating its ability to fully neutralize PTHrP function. There was no significant difference in the potency of the mouse, chimera, or the humanized antibodies to suppress the PTHrP-induced increase in the intracellular cAMP in ROS cells. Furthermore, at the same doses, the administration of the chimera or the humanized antibody was equally effective in reducing the blood ionized calcium levels of hypercalcemic mice bearing the PAN-7-JCK human pancreatic cancer xenograft or the LC-6-JCK human lung cancer xenograft that secreted PTHrP. Thus, humanized anti-PTHrP may be useful for the treatment of the humoral hypercalcemia of malignancy in humans.

L31 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 3

2003534792. PubMed ID: 14613038. Treatment of malignancy-associated hypercalcemia and cachexia with humanized anti-parathyroid hormone-related protein antibody. Sato Koh; Onuma Etsuro; Yocum Richard C; Ogata Etsuro. (Department of International Coordination, Chugai Pharmaceutical Co, Ltd, Skizuuoka, Japan.) Seminars in oncology, (2003 Oct) Vol. 30, No. 5 Suppl 16, pp. 167-73. Ref: 11. Journal code: 0420432. ISSN: 0093-7754. Pub. country: United States. Language: English.

AB Parathyroid hormone-related protein (PTHrP) plays a central role in humoral hypercalcemia of malignancy (HHM), which is one of the most frequent paraneoplastic syndromes. PTHrP produced by the tumor acts through a common PTH/PTHrP receptor to promote bone resorption, inhibit calcium excretion from the kidney, and induce hypercalcemia. Patients with HHM often develop cachexia associated with typical symptoms such as anorexia, malaise, nausea, constipation, polyuria, polydipsia, and confusion. The etiology of the cachexia is not fully understood but is thought to be caused by hypercalcemia and various cytokines such as interleukin-6, tumor necrosis factor-alpha, leukemia inhibitory factor, and others. In this study, we investigated the role of PTHrP in hypercalcemia and cachexia in HHM by using humanized anti-PTHrP antibody. A mouse monoclonal antibody that binds to PTHrP amino acid sequence 1-34 and inhibits PTHrP function has been humanized to create a specific and potent agent for the treatment of patients with HHM. The mouse monoclonal antibody has been shown to have antihypercalcemic activity against nude mice bearing human tumors. Because a mouse antibody is highly immunogenic in human patients, the complementarity-determining regions from the mouse antibody were grafted

into a human antibody. The resulting humanized antibody specifically recognizes PTHrP(1-34) and neutralizes PTHrP functions in vitro and in vivo. The humanized anti-PTHrP antibody was administered intravenously to HHM model animals bearing tumors such as LC-6 human lung carcinoma. These animals showed symptoms similar to those of patients with HHM (eg, hypercalcemia and cachexia). The humanized anti-PTHrP antibody-treated animals responded with normalization of blood ionized calcium level through an improvement of bone metabolism and calcium excretion. Moreover, the treated animals also showed an improvement in body weight, ultromotivity, metabolic alkalosis, food consumption, water intake, serum phosphorus, and renal function. Consequently, the humanized antibody-treated animals experienced complete resolution of hypercalcemia and cachexia. These results suggest that the humanized antibody would be an effective and beneficial agent for patients with HHM, and that PTHrP is a major pathogenetic factor of hypercalcemia and cachexia in patients with HHM.

L31 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 4

2003428817. PubMed ID: 12969787. Monoclonal antibody to parathyroid hormone-related protein induces differentiation and apoptosis of chondrosarcoma cells. Miyaji Takahiro; Nakase Takanobu; Onuma Eturo; Sato Koh; Myoui Akira; Tomita Tetsuya; Joyama Susumu; Ariga Kenta; Hashimoto Jun; Ueda Takafumi; Yoshikawa Hideki. (Department of Orthopaedic Surgery, Osaka University Medical School, 2-2 Yamadaoka, Suita 565-0871, Japan.. miyaji@ort.med.osaka-u.ac.jp) . Cancer letters, (2003 Sep 25) Vol. 199, No. 2, pp. 147-55. Journal code: 7600053. ISSN: 0304-3835. Pub. country: Ireland. Language: English.

AB We investigated the effects of treatment with anti-parathyroid hormone-related protein (1-34) monoclonal murine antibody (anti-PTHrP MoAb) on apoptosis and the differentiation of chondrosarcoma HTB-94 cells. Treatment with anti-PTHrP MoAb accelerated apoptosis of HTB-94 cells in a dose-dependent manner, and anti-PTHrP MoAb also promoted the chondrogenic differentiation of HTB-94 cells. The induction of apoptosis by anti-PTHrP MoAb via imbalance of Bcl-2/Bax ratio and activation of caspase-3 may provide a mechanistic explanation for its potential antitumor effects. Our results suggest the possibility that anti-PTHrP MoAb may be beneficial as a new treatment for chondrosarcoma.

L31 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

2001:31355 Document No. 134:99582 Remedies for drug-resistant hypercalcemia. Saito, Hidemi; Tsunenari, Toshiaki; Onuma, Etsuro (Chugai Seiyaku Kabushiki Kaisha, Japan). PCT Int. Appl. WO 2001002012 A1 20010111, 118 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP4523 20000706. PRIORITY: JP 1999-192270 19990706.

AB Remedies for drug-resistant hypercalcemia which contain as the active ingredient a substance inhibiting the binding of a parathyroid hormone-related peptide to its receptor. Therapeutics for drug-resistant hypercalcemia include bone resorption inhibitor.(e.g. bisphosphates and/or calcitonin), calcium excretion promoter, intestinal calcium absorption inhibitor, or loop diuretic. The PTHrP and receptor-binding inhibitors are PTHrP receptor antagonist such as anti-PTHrP antibodies or fragments or chimeric antibodies.

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